

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of:	)	
Meyskens, et al.	)	Art Unit: TBD
	)	
Application No.: To Be Determined	)	Examiner: TBD
	)	
Filed: February 17, 2004, Herewith	)	
	)	
For: Alpha-Difluoromethylornithine	)	
(DFMO) Suppresses Polyamine	)	
<u>Levels in the Human Prostate</u>	)	

**INFORMATION DISCLOSURE STATEMENT**

Mail Stop Patent Application  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Pursuant to 37 C.F.R Section 1.56, Applicants wish to call the attention of the Examiner to the references that are listed on the attached PTO forms 1449. No copies of the references are being provided per 37 C.F.R. 1.98(d), since all of the references were cited by or submitted to the Office in parent application Serial No. 09/938,846.

No representation is made that the references disclosed herein legally constitute prior art, or that more relevant references are not available. The disclosed references are printed in the English language and/or accompanied by an Abstract published in the English language.

The disclosed references, when taken alone or in combination, are not believed to disclose nor make obvious the invention as claimed in the subject application.

Respectfully submitted,

Dated: February 17, 2004



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Form PTO-1449 (modified)		Atty. Docket No. ILEX:053US	Serial No. 09/938,846
List of Patents and Publications for Applicant's  INFORMATION DISCLOSURE STATEMENT  (Use several sheets if necessary)		Applicant Frank L. Meyskens, Jr. <i>et al.</i>	
		Filing Date: August 24, 2001	Group: 1623
U.S. Patent Documents <i>See Page 1</i>	Foreign Patent Documents <i>See Page 1</i>	Other Art <i>See Page 1</i>	

### U.S. Patent Documents

Exam. Init.	Ref. Des.	Document Number	Date	Name	Class	Sub Class	Filing Date of App.
	A1	4,330,559	5/18/82	Bey <i>et al.</i>	424	319	2/3/81
	A2	4,413,141	11/1/83	Bey <i>et al.</i>	562	561	9/17/82
	A3	4,499,072	2/12/85	Sunkara <i>et al.</i>	424	85	1/24/83
	A4	4,859,452	8/22/89	Ajani <i>et al.</i>	424	10	1/13/87
	A5	4,925,835	5/15/90	Heston	514	183	10/26/87
	A6	5,002,879	3/26/91	Bowlin <i>et al.</i>	435	71.1	12/5/89
	A7	6,277,411 B1	7/10/01	Gerner <i>et al.</i>	514	544	3/26/99
	A8	6,258,845 B1	8/21/01	Shaked <i>et al.</i>	424	489	12/11/98

### Foreign Patent Documents

Exam. Init.	Ref. Des.	Document Number	Date	Country	Class	Sub Class	Translation Yes/No

### Other Art (Including Author, Title, Date Pertinent Pages, Etc.)

Exam. Init.	Ref. Des.	Citation
	C1	Auvinen, "Cell transformation, invasion and angiogenesis: a regulatory role for ornithine decarboxylase and polyamines?" <i>J. Natl Cancer Inst.</i> , 89:533-537, 1997.
	C2	Brawn <i>et al.</i> , "Prostatic acid phosphatase levels (enzymatic method) from completely sectioned, clinically benign, whole prostates," <i>The Prostate</i> , 28: 295-299, 1996.
	C3	Carbone <i>et al.</i> , "Phase I chemoprevention study of piroxicam and alpha-difluoromethylornithine." <i>Cancer Epidemiol Biomarkers Prev</i> 7(10): 907-912, 1998.
	C4	Carter <i>et al.</i> , "Prostate-specific membrane antigen is a hydrolase with substrate and pharmacologic characteristics of a neuropsptidase," <i>Proc. Nat'l Acad. Sci. USA</i> 93: 749-753, 1996.
	C5	Clifford <i>et al.</i> , "Role of ornithine decarboxylase in epidermal tumorigenesis," <i>Cancer Res.</i> , 55:1680-1686, 1995.

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Exam. Init.	Ref. Des.	Citation
	C6	Cote <i>et al.</i> , "The effect of finasteride on the prostate gland in men with elevated serum prostate specific antigen levels," <i>Br. J. Cancer</i> , 78(3):413-418, 1998.
	C7	Croghan <i>et al.</i> , "Dose-related $\alpha$ -difluoromethylornithine ototoxicity," <i>Am. J. Clin. Oncol.</i> , (14):331-335, 1991.
	C8	Danzin <i>et al.</i> , "Effect of $\alpha$ -difluoromethylornithine, an enzyme-activated irreversible inhibitor of ornithine decarboxylase, on polyamine levels in rat tissues," <i>Life Sci.</i> , 24:519-524, 1979.
	C9	Danzin <i>et al.</i> , "Effects of $\alpha$ -difluoromethylornithine, an enzyme-activated irreversible inhibitor of ornithine decarboxylase, on testosterone-induced regeneration of prostate and seminal vesicle in castrated rats," <i>Biochem. J.</i> , 180:507-513, 1979.
	C10	Dunzendorfer and Russell, "Altered polyamine profiles in prostatic hyperplasia and in kidney tumors," <i>Cancer Res.</i> , 38:2321-2324, 1978.
	C11	Feuer <i>et al.</i> , "Cancer surveillance series: interpreting trends in prostate cancer-part II: Cause of death misclassification and the recent rise and fall in prostate cancer mortality," <i>J. Natl Cancer Inst.</i> , 91(12):1025-1032, 1999.
	C12	Gerner <i>et al.</i> , "Gastrointestinal tissue polyamine contents of patients with Barretts esophagus treated with difluoromethylornithine," <i>Cancer Epidemiol. Biomarkers Prev.</i> , 3:325-330, 1994.
	C13	Heston <i>et al.</i> , "Copenhagen rat prostatic tumor ornithine decarboxylase activity (ODC) and the effect of the ODC inhibitor $\alpha$ -difluoromethylornithine," <i>The Prostate</i> , 3:383-389, 1982.
	C14	Jacoby <i>et al.</i> , "Chemopreventive efficacy of combined piroxicam and difluoromethylornithine treatment of Apc mutant Min mouse adenomas, and selective toxicity against Apc mutant embryos," <i>Cancer Research</i> , 60(7): 1864-1870, 2000.
	C15	Kergozien, "Polyamine deprivation provokes an antalgic effect," <i>Life Sci.</i> , 58(24):2209-2215, 1996.
	C16	Kubota <i>et al.</i> , "Ornithine decarboxylase overexpression in mouse 10T1/2 fibroblasts: cellular transformation and invasion," <i>J. Nat'l Cancer Inst.</i> , 89:567-571, 1997.
	C17	Kulkarni <i>et al.</i> , "Effect of the chemopreventive agents piroxicam and D,L- $\alpha$ -difluoromethylornithine on intermediate biomarkers of colon carcinogenesis," <i>Carcinogenesis</i> , 13:995-1000, 1992.

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Exam. Init.	Ref. Des.	Citation
	C18	Levin <i>et al.</i> , "Phase I-II study of eflornithine and mitogauzone combined in the treatment of recurrent primary brain tumors," <i>Cancer Treat. Rep.</i> , 71:459-464, 1987.
	C19	Li <i>et al.</i> , "Prevention by aspirin and its combination with alpha- difluoromethylornithine of azoxymethane-induced tumors, aberrant crypt foci and prostaglandin E2 levels in rat colon." <i>Carcinogenesis</i> 20(3): 425-430, 1999.
	C20	McCann and Pegg, "Ornithine decarboxylase as an enzyme target for therapy," <i>Pharmacol. Ther.</i> , 54:195-215, 1992.
	C21	Messing <i>et al.</i> , "Low dose difluoromethylornithine and polyamine levels in human prostate tissue," <i>J. Natl Cancer Inst.</i> , 91(16):1416-1417, 1999.
	C22	Meyskens and Gerner, "Development of difluoromethylornithine (DFMO) as a chemopreventive agent," <i>Clin. Cancer Res.</i> , 5:945-951, 1999.
	C23	Meyskens <i>et al.</i> , "A phase II study of $\alpha$ -difluoromethylornithine (DFMO) for the treatment of metastatic melanoma," <i>Invest. New Drugs</i> , (4):257-262, 1986.
	C24	Meyskens <i>et al.</i> , "Dose de-escalation chemoprevention trial $\alpha$ -difluoromethylornithine in patients with colon polyps," <i>J. Natl Cancer Inst.</i> , 86(15):1122-1130, 1994.
	C25	Meyskens <i>et al.</i> , "Effect of difluoromethylornithine on rectal mucosal levels of polyamines in a randomized, double-blind trial for colon cancer prevention" <i>J. Natl. Cancer Inst.</i> , 90(16):1212-1218, 1998.
	C26	Mitchell <i>et al.</i> , "Polyamine measurements in the uterine cervix," <i>J. Cell Biochem Suppl.</i> , 28/29:125-132, 1997.
	C27	Mohan <i>et al.</i> , "Over-expression of ornithine decarboxylase in prostate cancer and prostatic fluid in humans," <i>Clin. Cancer Res.</i> , 5:143-147, 1999.
	C28	Moulinoux <i>et al.</i> , "The growth of MAT-LyLu rat prostatic adenocarcinoma can be prevented <i>in vivo</i> by polyamine deprivation," <i>J. Urol.</i> , 146:1408-1412, 1991.
	C29	Nigro <i>et al.</i> , "Importance of the duration of inhibition on intestinal carcinogenesis by difluoromethylornithine in rats," <i>Cancer Lett.</i> , 35:153-158, 1987.
	C30	Nowels <i>et al.</i> , "Prevention of the inhibitory effects of alpha-diflouromethylornithine on rat urinary bladder carcinogenesis by exogenous putrescine", <i>Cancer. Biochem. Biophys.</i> , 8:257-263, 1986.

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Exam. Init.	Ref. Des.	Citation
	C31	Pegg, "Polyamine metabolism and its importance in neoplastic growth and a target for chemotherapy," <i>Cancer Res.</i> , 48:759-774, 1988.
	C32	Pienta <i>et al.</i> , "Phase II chemoprevention trial of oral fenretinide in patients at risk for adenocarcinoma of the prostate," <i>Am. J. Clin Oncol.</i> , 20(1):36-39, 1997.
	C33	Reddy <i>et al.</i> , "Chemoprevention of colon carcinogenesis by concurrent administration of piroxicam, a nonsteroidal anti-inflammatory drug with D,L- $\alpha$ -difluoromethylornithine, and ornithine decarboxylase inhibitor, in diet," <i>Cancer Res.</i> , (50):2562-2568, 1990.
	C34	Singh <i>et al.</i> , "Intermediate biomarkers of colon cancer, modulation of expression of ras oncogene by chemopreventive agents during azoxymethane induced colon carcinogenesis," <i>Carcinogenesis</i> , 14:669-704, 1993.
	C35	Thompson <i>et al.</i> , "Effect of concentration of D,L-2-Difluoromethylornithine on murine mammary carcinogenesis," <i>Cancer Res.</i> , 45:1170-1173, 1985.
	C36	Verma, "Inhibition of tumor promotion by DL-alpha-difluoromethylornithine, specific irreversible inhibitor of ornithine decarboxylase," <i>Basic Life Sci.</i> , 52:195-204, 1990.
	C37	Wallon <i>et al.</i> , "Polyamine-dependent expression of the matrix metalloproteinase matrilysin in a human colon cancer cell line," <i>Mol. Carcinog.</i> , 11:138-144, 1994.
	C38	Weeks <i>et al.</i> , " $\alpha$ - Difluoromethylornithine, an irreversible inhibitor of ornithine decarboxylase, inhibits tumor promoter-induced polyamine accumulation and carcinogenesis in mouse skin," <i>Proc. Nat'l Acad. Sci. U.S.A.</i> , (79):6028-6032, 1982.
	C39	Co-pending U.S. Patent Application Serial Number 09/801,197 filed March 6, 2001.

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